---Ain Shams University
Department of Tropical Medicine

Midodrine versus Albumin for prevention of paracentesis induced circulatory dysfunction (PICD)

Thesis

Submitted for Partial Fulfillment of Master Degree in
Tropical Medicine

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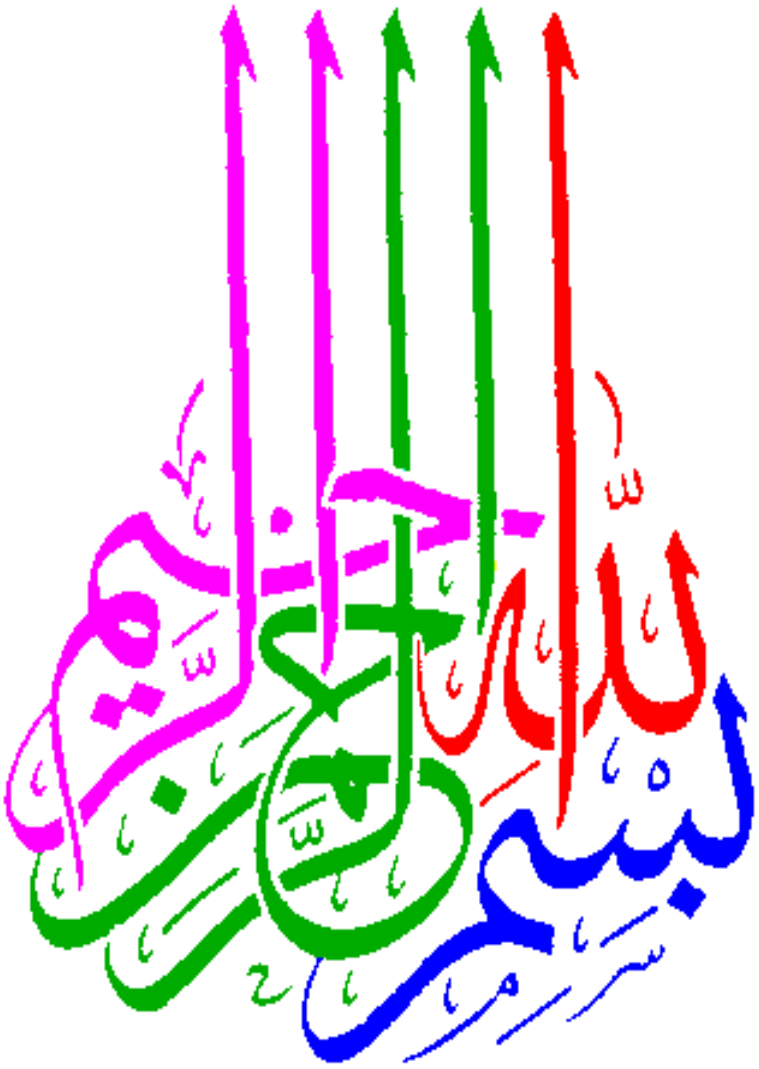
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Ahmed Osman Sleim

Dedication

TO MY FAMILY

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List of Abbreviations

ACE : Angiotensin-Converting Enzyme.

ACEI : Angiotensin-Converting Enzyme Inhibitor.

ACTH : Adrenocoricotrophic Hormone.

ADH : Antidiuretic Hormone.

Ang : Angiotensin.

ANP : Atrial Natriuretic Peptide.

AT١ : Angiotensin II type ١.

AT٣ : Angiotensin II type ٣.

AT٤ : Angiotensin II type ٤.

CNS : Central Nervous System.

COP : Cardiac Output.

CTGF : Connective Tissue Growth Factor.

ECG :Electrocardiogram.

EDTA : Ethylenediaminetetraacetic Acid.

ERK : Extracellular signal-regulated kinases.

GFR : Glomerular Filtration Rate.

HR : Heart rate.

HRS : Hepatorenal Syndrome.

IV : Intravenous.

JG : Juxtaglomerular Cells.

MAP : Mean Arterial Pressure.

NaCl : Sodium Chloride.

NADP : Nicotinamide Adenine Dinucleotide Phosphate.

NADPH : Reduced Nicotinamide Adenine Dinucleotide Phosphate.

PICD : Paracentesis-Induced Circulatory Dysfunction.

PRA : Plasma Renin Activity.

RAAS : Renin-Angiotensin-Aldosterone-System.

RNA : Ribonucleic Acid.

SAAG : Serum Ascites-Albumin Gradient.

SBP : Spontaneous Bacterial Peritonitis.

SMS : Somatostatin.

SVR : Systemic Vascular Resistance.

t.i.d : Three times daily.

TGFβ-١ : Transforming Growth Factor Beta-١.

UNa : Urinary Sodium Excretion.

VEGF : Vascular Endothelial Growth Factor.

VSMC : Vascular Smooth Muscle Cell.

Octreotide -LAR : Octreotide Acetate Injection

Introduction

Ascites is one of the most frequent and severe complications in patients with liver cirrhosis. Therapeutic paracentesis of ascites is an effective and safe therapy for refractory ascites ***(Gines et al., ١٩٨٧)***

Large-volume paracentesis in patients with cirrhosis and ascites induces arterial vasodilatation and decreases effective arterial blood volume, termed paracentesis-induced circulatory dysfunction ***(Appenrodt et al., ٢٠٠٨),*** which occurs ٤-٦ days after paracentesis ***(Simon et al., ١٩٨٧ and Ruiz-Del-Arbol et al., ١٩٩٧)***

It can be prevented by intravenous albumin however, its use is costly ***(Appenrodt et al., ٢٠٠٨ and Singh et al., ٢٠٠٨)***

Vasoconstrictors, e.g. terlipressin and midodrine, may also prevent paracentesis-induced circulatory dysfunction ***(Appenrodt et al., ٢٠٠٨).***

Midodrine is an alpha-agonist prodrug of desglymidodrine that has been reported to be of clinical benefit in patients with neurocardiogenic syncope ***(Appenrodt et al., ٢٠٠٨).***

There are few studies about use of midodrine in the prevention of paracentesis-induced circulatory dysfunction.

A study suggests that midodrine may be as effective as albumin in preventing paracentesis-induced circulatory dysfunction in cirrhotics, with fraction of the cost, besides it can be administered orally ***(Singh et al., ٢٠٠٨).***

But ***Appenrodt et al. (٢٠٠٨)*** suggest that midodrine is not as effective as albumin in preventing circulatory dysfunction after large-volume paracentesis in patients with cirrhosis and ascites.

Aim of work

To compare the effectiveness of the less expensive vasoconstrictor midodrine with albumin in preventing paracentesis-induced circulatory dysfunction

Patient and Methods

- **Study Design:** Cohort study.
- **Setting:** Ain Shams University Hospitals.
- **Patients:**
  - **No of patients:** ٥٠ patients.
  - **Inclusion criteria:**
    - Patients with cirrhosis or hepatic malignancy with tense ascites.
    - Tapping ≥ ٦ liters of ascetic fluid.
  - **Exclusion criteria:**
    - Hemodynamic unstablity.
    - Hepatic encephalopathy.
    - Pre-treatment systolic Hypertension (mean ١٧٠ mmHg).
    - Severe organic heart disease (coronary heart disease or congestive heart failure), renal impairment (>١,٥ mg/dL), urinary retention, pheochromocytoma or thyrotoxicosis (in patients treated with midodrine).
  - **Groups:**
    - **Group I:** ٢٥ Patients will be treated with midodrine (١٢,٥ mg three times per day; over ٣ days) after large-volume paracentesis.
    - **Group II:** ٢٥ Patients will be treated with albumin (٨ g/L of removed ascites) after large-volume paracentesis.

Albumin was given at a dose of ٨ g/L of ascetic fluid removed (mean ٤٨,٤ ± ١٢,١ g), Fifty percent of the dose was given within ٢ hours, and the remainder ٦ hours after the procedure.

Methods:

All patients will subjected to:

١. **Complete History Taking**
٢. **Thorough clinical examination:** with special stress on measurement of blood pressure and pulse (before and after paracentesis every ٨ hours for ٦ days).
٣. **Laboratory investigations:**
   - **Complete blood count (CBC):** haemoglobin concentration (Hb%), red blood cells (RBCs), white blood cells (WBCs), platelet count.
   - **Liver function tests:** alanine aminotransferase (ALT), aspartate aminotransferase (AST), total proteins, albumin, total and direct bilirubin, prothrombin time, and INR in addition to PTT.
   - **Renal function tests:** serum blood urea nitrogen (BUN), creatinine, sodium and potassium levels (before and ٦ days after paracentesis) and complete urine analysis.
   - **Ascitic fluid analysis:**
     i. **Chemistry:** including total proteins, albumin, serum ascites - albumin concentration gradient (SAAG) which was estimated as (serum albumin - ascitic fluid albumin) ,glucose and lactate dehydrogenase .

ii. **Total cell count and polymorphonuclear leukocytes count.**

- Plasma renin Activity (before and ٦ days after paracentesis) by Radioactive Immune Assay (RIA).
- Serum aldosterone level(before and ٦ days after paracentesis) by Radioactive Immune Assay (RIA).

٤. **Abdominal ultrasound.**

٥. **Large volume paracentesis** ≥ ٦ liters followed immediately by either midodrine or intravenous albumin infusion.

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Chapter ١

Ascites