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Fluid Management during liver transplantation

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بسم الله الرحمن الرحيم

وقُلِ اعْمَلُوا فَسَيَرَى اللَّهُ عَمَلَكُمْ ورَسُولُهُ والْمُؤْمِنُونَ

صدق الله العظيم

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Ahmed Nabil Mahmoud Mohamed

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List of Abbreviations

2D	:	Two dimensional
ACLF	:	Acute on chronic liver failure
ADH	:	Antidiuretic hormone
ALF	:	Acute liver failure
aPPT	:	Activated partial thromboplastin time
ASA	:	American Society of Anesthesiologists
ATP	:	Adenosine – triphosphate
Ca^{+}	:	Calcium
CAP	:	College of American pathologists
CCO	:	Continous cardiac output
Cl^{-}	:	Chloride
CO	:	Cardiac output
CVP	:	Central venous pressure
DIC	:	Disseminated intravascular coagulopathy
ECG	:	Electrocardiography
eNOS	:	Endothelial nitric oxide synthase
FFP	:	Fresh frozen plasma
FTc	:	Corrected flow time
GVHD	:	Graft versus host disease
HAV	:	Hepatitis A virus
HBV	:	Hepatitis B virus
HCC	:	Hepatocellular carcinoma
HCT	:	Hemotacrit
HCV	:	Hepatitis C virus
HDV	:	Hepatitis D virus
HES	:	Hydroxy ethyl starch solution
HEV	:	Hepatitis E virus
Hg	:	Hemoglobin
HMW	:	High Molecular weight
INR	:	International normalized ratio
IVV	:	Intravascular volume
K^{+}	:	Potassium
LA	:	lactated ringer
LDL	:	Low density lipoproteins

List of Abbreviations (Cont.)

LT	:	Liver transplantation
LV	:	Left ventricle
MA	:	Human albumin
MELD	:	Model for end-stage liver disease score
MRS	:	Hepatorenal syndrome
MW	:	Molecular weight
Na^+	:	Sodium
NAFLD	:	Non alcoholic fatty liver disease
NIBP	:	Non invasive blood pressure monitoring
NMELD	:	New model for end stage liver disease
NO	:	Nitric oxide
NS	:	Normal saline
OLT	:	Orthotopic liver transplantation
PAC	:	Pulmonary artery catheter
PAWP	:	Pulmonary artery wedge pressure
PCWP	:	Pulmonary catheter wedge pressure
PELD	:	Pediatric end-stage liver disease score
$PETCO_2$	:	End tidal carbon-dioxide tension
PICCO	:	Pulse indicator continuous cardiac output
PT	:	Prothrombin time
RAAS	:	Renin – angiotensin – aldosterone system
RBC	:	Red blood cells
rFVIIa	:	Recombinant factor VIIa
RMuEPO	:	Recombinant human erythropoietin
RV	:	Right ventricle
SNS	:	Sympathetic nervous system
SPO_2	:	Oxygen saturation
SVR	:	Systemic vascular resistance
TBW	:	Total body water
TED	:	Transesophageal Doppler
TEE	:	Transoesophageal echocardiography
TEG	:	Thromboelastography
TOE	:	Transoesophageal echocardiography
tPA	:	Tissue plasminogen activator
VLDL	:	Very low density lipoproteins

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Introduction

Liver transplantation remains one of the treatments for many life-threatening liver diseases. The first human liver transplantation was performed in 1963 in Denver, Colorado. Around 350 liver transplants have been performed from 1995 to 2011 in India. One-year survival post-liver transplant has increased from 72% to 79% in 1998 to 85% to 90% in 2008. Ten-year survival has increased from 33% in 1998 to 53% in 2008 and 66% in 2010. **(Epub et al., 2010)**

Liver transplant surgery is associated with massive fluid shifts, both from the perspective of intravascular volume depletion and large surgical blood loss. Albumin can be used in liver transplants as the patients are often hypoalbuminaemic and hypovolaemic. The use of hydroxyl ethyl starches (modern low-molecular weight) and Gelatins in liver transplant have not been supported by convincing evidence. Furthermore, these may affect the coagulation profile and possess a risk to increased renal injury. **(Costa et al., 2011)**

The selection of various crystalloids during liver transplantation should be based on their pH, electrolyte composition, osmolarity and metabolism. There is no ideal crystalloid solution and all have limitations; normal saline (0.9% NS) causes hyperchloremic acidosis while the lactate in Ringer Lactate (RL) requires liver metabolism for its elimination. **(Sabate et al., 2012)**

Renal Insufficiency (RI) is a common finding in patients suffering from end-stage liver disease. The causes of RI are reported to be multifactorial and the degree of RI can range from early functional impairment to hepatorenal syndrome (HRS). The process of liver transplantation is highly likely to exacerbate the symptoms and sequelae of renal dysfunction. RI continues to be a cause of morbidity and mortality in the intraoperative and postoperative periods.

(Wellman et al., 2012)

The Problem of massive blood loss during hepatic resection and liver transplantation is an important problem for surgeons and anesthesiologists alike. As a result, a variety of strategies have been developed to limit the degree of blood loss, including use of autotransfusion devices, acute isovolemic hemodilution and a variety of surgical maneuvers. In addition, a strategy of maintaining relative hypovolemia has been proposed and strongly advocated by some investigators. In several nonrandomized retrospective studies of liver resections, lowering the central venous pressure (CVP) to less than 5 mmHg, with or without some sort of portal triad clamping, was associated with decreased intraoperative blood loss and even decreased morbidity and hospital stays.

(Rebecca et al., 2004)

Despite success in lowering blood transfusion requirements in liver resection patients, low CVP should be avoided in patients under going liver transplantation.

(Bradley et al., 2004)

Liver transplantation was associated with massive blood transfusions in the past. The typical RBCs requirement per adult liver transplant recipient were between 10 and 20 units of RBCs in most centers. The variability between transplant centers in the amount and type of blood products used may be due to differences in patient populations, surgical techniques and transfusion practices at each institution .Average blood requirements are now considerably lower with median transfusion rates between 1 and 3 units. Several patients have undergone successful transplantation without any transfusion. In fact, some centers have developed programs specifically for patients who refuse all blood products. **(Rockvill et al., 2006)**

The intraoperative management of liver transplant patients is not uniform between institutions and is often dictated by local practice patterns. This variety reflects, in part, the lack of good outcome studies. Recent studies about

coagulation monitoring, transfusion triggers and fluid management have challenged the ingrained practice patterns and may allow transplant centers to draft best practices.

(Schumann et al., 2003)

Aim of The Work

The purpose of this essay is to focus on the most recent trends in the management of fluids in patients undergoing liver transplantation.

Chapter 1

Pathophysiology of cardiovascular, renal and hepatic systems in liver transplantation

The liver, weighing roughly 1.2-1.6 kg, performs many of the functions necessary for staying healthy. It is located in the right side of the body under the lower ribs and is divided into four lobes of unequal size. Two large vessels carry blood to the liver. The hepatic artery comes from the heart and carries blood rich in oxygen. The portal vein brings the liver blood rich in nutrients absorbed from the small intestine. These vessels divide into smaller and smaller vessels, ending in capillaries. These capillaries end in the thousands of lobules of the liver. Each lobule is composed of hepatocytes, and as blood passes through, they are able to monitor, add and remove substances from it. The blood then leaves the liver via the hepatic vein, returns to the heart and is ready to be pumped to the rest of the body. **(Tzanakakis et al., 2000)**

Physiological Consideration of Normal Liver:

As a result of its large and diverse enzymatic content and its unique structure, and because it receives venous blood from the intestine, the liver has a wider variety of functions than any other organ in the body these functions include:

1- ***Removing and excreting body wastes and hormones as well as drugs and other foreign substances***: These substances have entered the blood supply either through production by metabolism within the body or from the outside in the form of drugs or other foreign compounds. Enzymes in the liver alter some toxins so they can be more easily excreted in urine.

2- ***Synthesizing plasma proteins, including those necessary for blood clotting***: Most of the 12 clotting factors are plasma proteins produced by the liver. If the liver is damaged or diseased, it can take longer for the body to form clots. Other plasma proteins produced by the liver include albumin which binds many water-insoluble substances and contributes to osmotic pressure, fibrogen

which is key to the clotting process and certain globulins which transport substances such as cholesterol and iron. **(Fox et al., 2003)**

3- ***Producing immune factors and removing bacteria, helping the body fight infection***: The phagocytes in the liver produce acute-phase proteins in response to microbes. These proteins are associated with the inflammation process, tissue repair and immune cell activities.

4- ***Producing bile to aid in digestion***: Bile salts aid in fat digestion and absorption. Bile is continuously secreted by the liver and stored in the gallbladder until a meal, when bile enters the beginning of the small intestine. Bile production ranges from 250 mL to 1 L per day depending on the amount of the food eaten. **(Fox et al., 2003)**

5- ***Excretion of bilirubin***: It is one of the few waste products excreted in bile. Macrophages in the liver remove worn out red blood cells from the blood. Bilirubin then results from the breakdown of the hemoglobin in the red blood cells and is excreted into bile by hepatocytes. Jaundice results when bilirubin cannot be removed from the blood quickly enough due to gallstones, liver disease, or the excessive breakdown of red blood cells.

6- ***Storing certain vitamins, minerals, and sugars***: The liver stores enough glucose in the form of glycogen to provide about a day's worth of energy. The liver also stores fats, iron, copper, and many vitamins including vitamins A, D, K and B12.

7- ***Processing nutrients absorbed from digestive tract***: The liver converts glucose into glycogen, its storage form. This glycogen can then be transformed back into glucose if the body needs energy. The fatty acids produced by the