RENAL PROTECTION IN MAJOR HEPATIC SURGERIES

An Essay
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Abstract

There appears to be no single therapy that will prevent perioperative acute kidney injury. It is more likely that we will reduce perioperative AKI through better optimization and management of the many comorbidities and hemodynamic derangements that have been shown to impact renal function. The perioperative period is an ideal time to prospectively study our preventive and therapeutic interventions for AKI.

Acute kidney injury (AKI) has significant prognostic implications for long-term outcomes in patients undergoing major liver surgeries. Hence, every effort has to be undertaken to preserve renal function throughout all stages of patient care.

Current diagnostic parameters for AKI are limited by reliance on serum creatinine, which is affected by age, gender and muscle mass. It is not so helpful in early detection of AKI as elevations in serum creatinine may occur several days after the actual injury. The search for AKI biomarkers has focused on identifying alternatives to serum creatinine. Urinary neutrophil gelatinase associated lipocalin (NGAL) and interleukin-18 may provide insights into the cause of AKI. Similarly, serum NGAL, serum cystatin C and urinary kidney injury molecule-1 (KIM-1) may facilitate the early diagnosis of AKI.

Key Words :

Major Hepatic Surgeries - Renal Protection .

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List of Abbreviations

^{99m}Tc-DMSA	**T**echnetium-**L**abeled **D**imer**c**apto**s**uccinic **A**cid
^{99m}Tc-DTPA	**T**echnetium-**L**abeled **D**iethylene**t**riamine **P**enta **A**cetic acid
ACEIs	**A**ngiotensin **C**onverting **E**nzyme **I**nhibitors
ADH	**A**nti-**D**iuretic **H**ormone
AKI	**A**cute **K**idney **I**njury
AKIN	**A**cute **K**idney **I**njury **N**etwork
ALF	**A**cute **L**iver **F**ailure
ALP	**Al**kaline **P**hosphatase
ALT	**Al**anine **T**ransaminase
ANP	**A**trial **N**atriuretic **P**eptide
ARBs	**A**ngiotensin **R**eceptor **B**lockers
ARF	**A**cute **R**enal **F**ailure
AST	**As**partate **T**ransaminase
ASAT	**As**partate **A**mino**t**ransferase
ATN	**A**cute **T**ubular **N**ecrosis
AVP	**A**rginine-**V**asopresin
BUN	**B**lood **U**rea **N**itrogen
Ca^{+2}	**Ca**lcium
CCBs	**C**alcium **C**hannel **B**lockers
CCO	**C**ontinuous **C**ardiac **O**utput
CKD	**C**hronic **K**idney **D**isease
Cl^{-}	**C**hloride
CMOAT	**C**analicular **M**ultispecific **O**rganic **A**nion **T**ransporter
CNI	**C**alcineurin **I**nhibitors

CNS	**C**entral **N**ervous **S**ystem
CRRT	**C**ontinuous **R**enal **R**eplacement **T**herapy
CT	**C**omputed **T**omography
CVVH	**C**ontinuous **V**eno**v**enous **H**emofiltration
CVVHD	**C**ontinuous **V**eno**v**enous **H**emo**d**ialysis
CVVHDF	**C**ontinuous **V**eno**v**enous **H**emo**d**ia**f**iltration
DIC	**D**isseminated **I**ntravascular **C**oagulopathy
ECF	**E**xtra**c**ellular **F**luid
FDA	**F**ood & **D**rug **A**dminstration
FHF	**F**ulminant **H**epatic **F**ailure
GFR	**G**lomerular **F**iltration **R**ate
GGT	**G**amma **G**lutamyl **T**ranspeptidase
HCC	**H**epato**c**ellular **C**arcinoma
HD	**H**emo**d**ialysis
HPS	**H**epato**p**ulmonary **S**yndrome
HRS	**H**epato**r**enal **S**yndrome
Ig	**I**mmuno**g**lobulin
IGF-1	**I**nsulin like **g**rowth **F**actor-1
IHD	**I**ntermittent **H**emo**d**ialysis
IL-18	**I**nter**l**eukin-18
IV	**I**ntra**v**enous
IVP	**I**ntra**v**enous **P**yelogram
JGA	**J**uxta-**g**lomerular **A**pparatus
K^+	Potassium
K_{ATP}	ATP sensitive potassium channel
KIM-1	**K**idney **I**njury **M**olecule -1
LDH	**L**actate **D**e**h**ydrogenase
MAP	**M**ean **A**rterial Blood **P**ressure
MELD	**M**odel for **E**nd-Stage **L**iver **D**isease

Mg^{+2}	Magnesium
MRI	**M**agnetic **R**esonance **I**maging
mRNA	**M**essenger **R**ibo**n**ucle**i**c **A**cid
MSCs	**M**esenchymal **S**tromal **C**ells
Na^{+}	Sodium
NAC	**N**-**A**cetyl **C**ysteine
NGAL	**N**eutrophil **G**elatinase-**A**ssociated **L**ipocalin
NHE3	**N**a-**H** **E**xchanger isoform 3
$NKCC_2$	**N**a-**K**-**C**l **C**otransporter 2
NSAIDs	**N**on-**S**teroidal **A**nti **I**nflamatory **D**rugs
PAC	**P**ulmonary **A**rtery **C**atheter
PCT	**T**he **P**roximal **C**onvoluted **T**ubule
PD	**P**eritoneal **D**ialysis
PGD_2	**P**rosta**g**landin **D_2**
PGE_1	**A**lprostadil
PGE_2	**P**rosta**g**landin **E_2**
PGI_2	**P**rostacyclin
RAAS	**R**enin-**A**ngiotensin-**A**ldosterone **S**ystem
RBF	**R**enal **B**lood **F**low
RBP	**R**etinol-**B**inding **P**rotein
RCRI	**R**evised **C**ardiac **R**isk **I**ndex
RCT	**R**andomized **C**ontrolled **T**rial
RIFLE	**R**isk, **I**njury, **F**ailure, **L**oss, **E**nd stage
RPF	**R**enal **P**lasma **F**low
RRT	**R**enal **R**eplacement **T**herapy
S.Cr	**S**erum **Cr**eatinine
SGLT	**S**odium **Gl**ucose co**t**ransporter
SGOT	**S**erum **G**lutamic **O**xaloacetic **T**ransaminase
SLED	**S**ustained **L**ow **E**fficiency **D**ialysis

SNS	**S**ympathetic **N**ervous **S**ystem
SVR	**S**ystemic **V**ascular **R**esistance
TAL	**T**hick **A**scending **L**imb
TEE	**T**rans-**e**sophageal **E**chocardiography
TIPS	**T**rans-jugular **I**ntrahepatic **P**ortosystemic **S**hunt
UFH	**U**n**f**ractionated **H**eparin
UO	**U**rine **O**utput
WBCs	**W**hite **B**lood **C**ells

Aim of the work

The main aim of this essay is to enable practitioners to make informed evidence based decisions on the updated anesthetic strategies that ensures renal protection in major hepatic surgeries.

Introduction

A priority for anesthesia care providers is to limit perioperative renal impairment. This process begins with the identification of patients at increased risk for perioperative renal dysfunction, understanding basic renal physiology and the influence of perioperative events and drugs on the pathophysiology of renal function. **(Elizabeth., 2006)**

Acute kidney injury is one of the most common complications of Major liver surgeries. It occurs more frequently in those who have hepatorenal syndrome at the time of surgery. Acute renal dysfunction has been associated with an 8-fold increase in mortality risk, prolonged intensive care unit stay and a greater risk for infectious complications. In the subgroup of patients who develop acute renal failure and survive, 80% to 90% regain some degree of renal function, whereas the rest develop permanent renal dysfunction. Chronic renal dysfunction, not only has implications in terms of an increased demand on resources, but is also significantly associated with a higher patient mortality rate. **(Smith., 2006)**

In this review, we discuss the various definitions, diagnostic tools, predictors of renal dysfunction after major liver surgery together with discussion of specific causes of renal dysfunction. This information will be useful in developing strategies for preventing the development or progression of renal dysfunction in liver surgery patients. **(Smith., 2006)**

Renal Physioloy

The kidneys play a vital role in regulating the volume and composition of body fluids, eliminating toxins, and elaborating hormones, including renin, erythropoietin, and the active form of vitamin D. Factors directly and indirectly related to operative procedures and to anesthetic management frequently have a physiologically significant impact on renal physiology and renal function, and may lead to perioperative fluid overload, hypovolemia, renal insufficiency, and kidney failure, which are major causes of perioperative morbidity and mortality. Each kidney is made up of approximately 1 million functional units called nephron.

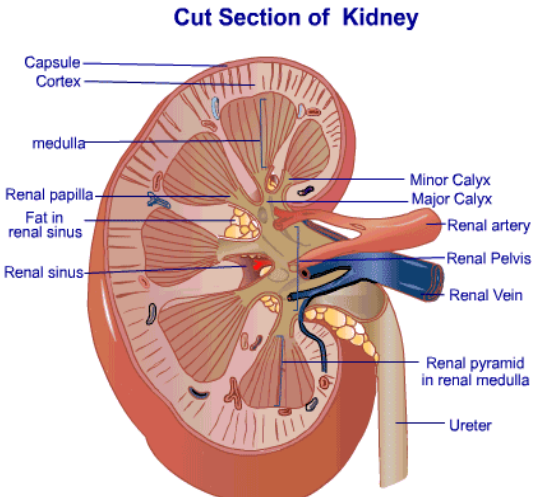

Fig. 1 : Structure of the kidney

(Cotran et al., 2005)

Anatomically, a nephron consists of a tortuous tubule with at least six specialized segments. At its proximal end (Bowmans capsule), an ultrafiltrate of blood is formed, and as this fluid passes through the nephron, its volume and composition are modified by both reabsorption and secretion of solutes. The final product is eliminated as urine. The six major anatomical and functional divisions of the nephron are the renal corpuscle, the proximal convoluted tubule, the loop of Henle, the distal renal tubule, the collecting tubule, and the juxtaglomerular apparatus. **(Ganong, 2001)**

The kidneys play an important dominant role in regulating the composition and volume of the extracellular fluid (ECF). They normally maintain a stable internal environment by excreting in the urine appropriate amounts of many substances. The kidneys perform a variety of important functions like the regulation of the osmolality of the body fluids, regulation of arterial blood pressure by Na+ excretion, maintaining acid-base balance by H+ execration and ammonia production, elimination of waste products of metabolism & elimination of many drugs & toxic compounds. They are also the major sites of production of certain hormones, including erythropoietin and 1,25-dihydroxy vitamin D3. **(Rhoades *et al.*, 2009)**

Renal blood flow (RBF)

Renal blood flow is approximately 1200 ml/min. (400ml/100g tissue/min). Under basal conditions, the total renal blood flow is approximately 20% of the resting cardiac output. **(Bullock, 2001)**

Control of renal blood flow

Regulation of renal perfusion involves a complex interplay between local and systemic factors (sympathetic nervous system, circulating hormones and auto-regulation of renal blood flow). **(David *et al.*, 2002)**

Vasoconstricting factors

The kidney is richly innervated by the sympathetic nervous system. Increased sympathetic activity causes constriction of the afferent and efferent arterioles and thus a decrease in renal blood flow. Intense sympathetic stimulation which occurs in shock and trauma can produce marked decreases in RBF and Glomerular Filtration Rate (GFR), even to the extent of causing blood flow to

cease altogether.Several humoral substances, including angiotensin II, Antidiuretic Hormone (ADH), and the endothelins, produce vasoconstriction of renal vessels. **(Porth *et al.*, 2010)**

Vasodilating factors

Other substances such as dopamine, nitric oxide, and prostaglandins produce vasodilation. Prostaglandins are a group of mediators of cell function that are produced locally and exert their effect locally. **(Porth *et al.*, 2010)**

Auto-regulation

The constancy of renal blood RBF is maintained by a process called auto-regulation, which maintains blood flow at a level consistent with the metabolic needs of the tissues. For auto-regulation to occur, the resistance to blood flow through the kidneys must be varied in direct proportion to the arterial pressure. The exact mechanisms responsible for the intra renal regulation of blood flow are unclear. One of the proposed mechanisms is a direct effect on vascular smooth muscle that causes the blood vessels to relax when there is an increase in blood pressure and to constrict when there is a decrease in pressure. **(Porth *et al.*, 2010)**

A second proposed mechanism is the juxtaglomerular apparatus (JGA). The juxtaglomerular complex is thought to represent a feedback control system that links changes in GFR with renal blood flow. It is thought to monitor the systemic arterial blood pressure by sensing the stretch of the afferent arteriole and the concentration of sodium chloride in the tubular fluid as it passes through the macula densa. This information is then used in determining how much renin should be released to keep the arterial blood pressure within its normal range and maintain a relatively constant GFR. The juxtaglomerular cells, contain granules of inactive renin, an enzyme that functions in the conversion of angiotensinogen to angiotensin. Renin functions by means of angiotensin II to produce