Non renal indications of Renal replacement therapy

Essay

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رسالة

توطئة للحصول على درجة الماجستير
فى الرعاية المركزة

مقدمة من

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Tamer M. Abd El Azim

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List of abbreviations

ADH	Antidiuretic hormone
ADHF	Acute decompensated heart failure
AKI	Acute kidney injury
ALI	Acute lung injury
APC	Activated protein-C
ARDS	Acute respiratory distress syndrome
ARF	Acute renal failure
ATP	Adenosine triphosphate
BCAAs	Branched-chain amino acids
BCKD	Branched-chain keto acid dehydrogenase
BNP	Brain-type natriuretic peptide
C3	Complement-3
C5	Complement-5
CARS	Counter inflammatory response syndrome
CAVH	Continuous arteriovenous hemofiltration
CAVHD	Continuous arteriovenous hemodialysis
CAVHDF	Continuous arteriovenous hemodiafiltration
CHF	Congestive heart failure
CHFD	Continuous high-flux dialysis
CoA	Coenzyme A
CPB	Cardiopulmonary bypass
CPS	Carbamoyl phosphate synthetase
CRP	C-reactive protein
CRRT	Continuous renal replacement therapy
CUF	Conventionel ultrafilteration
CVVH	Continuous venovenous hemofiltration
CVVHD	Continuous venovenous hemodialysis
CVVHDF	Continuous venovenous hemodiafiltration
EAV	Effective arterial volume
EBP	Extracorporeal blood purification
ECF	Extracellular fluid
ECMO	Extracorporeal mechanical oxygenation
ECUF	Extracorporeal ultrafiltration
EDD	Extended daily dialysis
EF	Ejection fraction

ESRD	End-stage renal disease
GFR	Glomerular filtration rate
HCO	high-cutoff
HVHF	High-volume hemofiltration
ICF	Intracellular fluid
ICU	Intensive care unit
IHD	Intermittent hemodialysis
IHF	Intermittent hemodiafiltration
IL-1	Interleukin-1
IL-6	Interleukin-6
IL-8	Interleukin-8
IUF	Intermittent ultrafiltration
IVA	Isovaleric aciduria
MMA	Methylmalonic aciduria
MSUD	Maple syrup urine disease
MUF	Modified ultrafilteration
NAGS	N-acetylglutamate synthetase
NF-kB	Nuclear factor-kB
NYHA	New York Heart Association
OTC	Ornithine transcarbamoylase
PA	Propionic aciduria
PD	Peritoneal dialysis
RAAS	Renin-angiotensin-aldosterone system
RRT	Renal replacement therapy
SCD	Slow continuous dialysis
SCUF	Slow, continuous ultrafiltration
SIRS	Systemic inflammatory response syndrome
SLED	Slow, low-efficiency dialysis
TBW	Total body water
TLS	Tumor lysis syndrome
TNF- a	Tissue necrosis factor- a

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Introduction

While there is clear support for the use of renal replacement therapy (RRT) in critically ill renal failure r patients, there are other illnesses without renal involvement where RRT might be of value.

Sepsis and other inflammatory syndromes represent the most comon non-renal indications for RRT. The underlying hypothesis is that hemofiltration removes inflammatory mediators (cytokines, complement activation products, contact activation products, arachidonic acid metabolites, and so forth) from the circulation and thereby dampens the systemic inflammatory response while preserving the local effects that are thought to be beneficial.***(Schetz, etal 1998)***.

In Acute Respiratory Distress Syndrome , Beside the eventual elimination of inflammatory mediators, fluid removal with reduction of extravascular lung water (EVLW) is a second mechanism by which hemofiltration may be beneficial in ARDS***(Moonka, Gentilello etal 1996).***

Another possible indication for hemofiltration is surgery with cardiopulmonary bypass (CPB). CPB, especially in children, results in tissue edema, pulmonary dysfunction, and poor cardiac performance caused by hemodilution and fluid overload and to activation of the inflammatory response. Isolated ultrafiltration, during and especially after CPB, in children has been shown to reduce weight gain, blood loss, and transfusion requirement, to improve left ventricular systolic and diastolic function, to decrease pulmonary vascular resistance and to improve oxygenation ***(Davies, Nguyen,etal 1998).***

In congestive heart failure (CHF) Some patients remain refractory to medical treatment, and in these patients, the removal of fluids and

sodium can be achieved with simple ultrafiltration. (***Canaud, Leray-Moragues,etal 1996***).

A few case reports suggest that hemofiltration, by extracorporeal elimination of lactate, may contribute to the correction of lactic acidosis ***(Hilton, Taylor, etal 1998).***

Because the molecular weight of myoglobin is 17,000 Da and thus compatible with convective removal, hemofiltration might represent a means to prevent renal failure in crush injury and other causes of rhabdomyolysis and myoglobin gaining access to the circulation***. (Nicolau, Feng,etal 1996)***.

Tumor lysis syndrome may lead to renal failure caused by tubular obstruction by uric acid crystals or to hyperphosphatemia with precipitation of calcium/phosphate complexes in renal interstitium and tubuli so, hemofiltration might represent a mean to prevent renal failure . ***(Pichette,Leblanc,etal1994).***

Aim of Work

Is to review use of renal replacement therapy (RRT)
In critically ill patients without renal involvement where RRT might be of value.

Physiological Aspects

The non renal indication of renal replacement therapy is based on the elimination of inflammatory mediators such as [systemic inflammatory response syndrome(SIRS) ,and sepsis , acute respiratory distress syndrome (ARDS), and cardiopulmonary bypass (CPB)] , on the removal of fluid (ARDS, CPB, heart failure), or on the elimination of other endogenous toxic solutes (inborn error of metabolism ,lactic acidosis , crush injury , tumor lysis syndrome).

That is why we will discuss the physiology of ;

1- Inflammation and inflammatory mediators

2- Body fluids

Physiology of inflammation and inflammatory mediators

Inflammation is the body's response to nonspecific insults that arise from chemical, traumatic, or infectious stimuli ***(Steven et al., 2007) .***

The inflammatory cascade is a complex process that involves humoral and cellular responses, complement, and cytokine cascades.

The relationship between these complex interactions and The inflammatory cascade summarized as the following 3-stage process:

Stage I: Following an insult, local cytokine is produced with the goal of inciting an inflammatory response, thereby promoting wound repair and recruitment of the reticular endothelial system***(Casey ,2000).***

Stage II: Small quantities of local cytokines are released into circulation to improve the local response. This leads to growth factor stimulation and the recruitment of macrophages and platelets. This acute phase response is typically well controlled by a decrease in the proinflammatory mediators and by the release of endogenous antagonists. The goal is homeostasis.

Stage III: If homeostasis is not restored, a significant systemic reaction occurs. The cytokine release leads to destruction rather than protection. A consequence of this is the activation of numerous humoral cascades and the activation of the reticular endothelial system and subsequent loss of circulatory integrity and lead to end organ dysfunction ***(Fry ,2000).***

Trauma, inflammation, or infection leads to the activation of the inflammatory cascade. When Systemic Inflammatory Response Syndrome (SIRS) is mediated by an infectious insult, the inflammatory cascade is often initiated by endotoxin or exotoxin. Tissue macrophages, monocytes, mast cells, platelets, and endothelial cells are able to produce a multitude of cytokines ***(Deans et al., 2005).***

The cytokines tissue necrosis factor-a (TNF-a) and interleukin (IL)–1 are released first and initiate several cascades. The release of IL-1 and TNF-a (or the presence of endotoxin or exotoxin) leads to cleavage of the nuclear factor-kB (NF-kB) inhibitor. Once the inhibitor is removed, NF-B is able to initiate the production of mRNA, which induces the production of other proinflammatory cytokines***(Dremsizov et al., 2006)***

IL-6, IL-8, and interferon gamma are the primary proinflammatory mediators induced by NF-kB . IL-6, stimulate the release of acute-phase reactants such as C-reactive protein (CRP).

IL-8 activates passage of leucocytes from circulation to degranulate and cause tissue damage

interferon gamma work as

- activate the pathway lead to cytotoxic T cell
- augmemt TNF-a activity.
- Induce nitrous oxide
- Upregulate vascular endothelial adhesion molecule ***(Deans et al., 2005) .***

The proinflammatory interleukins either function directly on tissue or work via secondary mediators to activate the coagulation cascade, complement cascade, and the release of nitric oxide, platelet-activating factor, prostaglandins, and leukotrienes.

Numerous proinflammatory polypeptides are found within the complement cascade. Protein complements C3a and C5a have been the most studied and are felt to contribute directly to the release of additional cytokines and to cause vasodilatation and increasing vascular permeability ***(David et al., 2003) .***

IL-1 and TNF-a directly affect endothelial surfaces, leading to the expression of tissue factor. Tissue factor initiates the production of thrombin, thereby promoting coagulation, and is a proinflammatory mediator itself. Fibrinolysis is impaired by IL-1 and TNF-a via production of plasminogen activator inhibitor-1. Proinflammatory

cytokines also disrupt the naturally occurring anti-inflammatory mediator's antithrombin and activated protein-C (APC). If unchecked, this coagulation cascade leads to complications of microvascular thrombosis, including organ dysfunction ***(Dellinger ,2003).***

The cumulative effect of this inflammatory cascade is an unbalanced state with inflammation and coagulation dominating. To counteract the acute inflammatory response, the body is equipped to reverse this process via counter inflammatory response syndrome (CARS) ***(Steven et al., 2007) .***

IL-4 and IL-10 are cytokines responsible for decreasing the production of TNF-a, IL-1, IL-6, and IL-8. The acute phase response also produces antagonists to TNF-a and IL-1 receptors.These antagonists either bind the cytokine, and thereby inactivate it, or block the receptors ***(Shapiro et al., 2006) .***

The balance of SIRS and CARS determines a patient's prognosis after an insult. Some researchers believe that, because of CARS, many of the new medications meant to inhibit the proinflammatory mediators may lead to deleterious immunosuppression ***(Dremsizov et al., 2006) .***