RENAL REPLACEMENT THERAPY IN CRITICALLY ILL PATIENTS

Essay

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INTRODUCTION

The prevalence of acute renal failure in critically ill patients remains high and mortality is up to 60%. Both the practice of renal replacement therapy (continuous against intermittent, hemofiltration against hemodialysis) and patient outcomes vary widely between studies. In most developed countries, the prevalence of acute renal failure (ARF) in critically ill patients ranges from 1 to 25%. Approximately 4% of this group receive renal replacement therapy (RRT) and the hospital mortality is up to 60% ***(Ricci et al., 2006).***

Different RRT strategies, like intermittent hemodialysis, continuous venovenous hemofiltration, or hybrid forms that combine the advantages of both techniques, are available. Since a general survival benefit has not been demonstrated for either method, it is the task of the nephrologist or intensivist to choose the RRT strategy that is most advantageous for each individual patient. The underlying disease, its severity and stage, the etiology of ARF, the clinical and the different costs of therapy may all influence the choice of the RRT strategy ***(Bagshaw et al., 2007).***

For many years, intermittent hemodialysis (IHD) was the only treatment option for patients with ARF in the ICU. In numerous countries, it is still the most frequently used modality. One problem with standard IHD was that it could not be used in patients with severe hemodynamic instability. This

led to the development of continuous RRT (CRRT). Continuous venovenous hemofiltration (CVVH) was subsequently proposed as an alternative to IHD in the critically ill, because it was better tolerated by hypotensive patients, and the continuous regulation of fluid and nutritional support avoided cycles of volume overload and depletion ***(Clark et al., 2003)***.

Continuous renal replacement therapy (CRRT) in pediatric acute kidney dysfunction has evolved in recent decades; however, little objective data exist for complications associated with CRRT. Santiago and colleagues are among the first to document four complications of acute kidney dysfunction in critically ill patient: catheterization-related insertion complications, hypotension, hemorrhage, and electrolyte disturbances. They reported that hypotension at connection (41.3%) and electrolyte disturbance (50.6%) were the leading complications. Although this study is limited by small sample size and the outcome variables measured, it is an important first step in assessing outcomes of CRRT. A prospective multicenter randomized trial ill be needed to fully delineate the complications and define the risk/benefit ratio of CRRT ***(Santiago et al., 2009).***

AIM OF THE WORK

The aim of this work is to provide updated information about renal replacement therapy in critically ill patients as regards techniques, indications and complication.

PRINCIPLES AND TECHNIQUES OF RENAL REPLACEMENT THERAPY

Anatomy of the kidney:

Kidneys are located in the abdominal cavity, more specifically in the paravertebral gutter and lie in a retroperitoneal position at a slightly oblique angle. There are two, one on each side of the spine. The asymmetry within the abdominal cavity caused by the liver typically results in the right kidney being slightly lower than the left, and left kidney being located slightly more medial than the right. The left kidney is typically slightly larger than the right ***(Cotran et al., 2005 and Glodny et al., 2009).***

The kidney has a bean-shaped structure; each kidney has a convex and concave surface. The concave surface, the renal hilum, is the point at which the renal artery enters the organ, and the renal vein and ureter leave. The kidney is surrounded by tough fibrous tissue, the renal capsule, which is itself surrounded by perinephric fat, renal fascia (of Gerota) and paranephric fat. The anterior (front) border of these tissues is the peritoneum, while the posterior border is the transversalis fascia. The superior border of the right kidney is adjacent to the liver and to the spleen. Therefore, both move down on inhalation. The kidney is approximately 11-14 cm in length, 6 cm wide and 4 cm thick ***(Glodny et al., 2009)***.

The substance, or parenchyma, of the kidney is divided into two major structures: superficial is the renal cortex and deep is the renal medulla. Grossly, these structures take the shape of 8 to 18 cone-shaped renal lobes, each containing renal cortex surrounding a portion of medulla called a renal pyramid (of Malpighi) ***(Walter, 2004).***

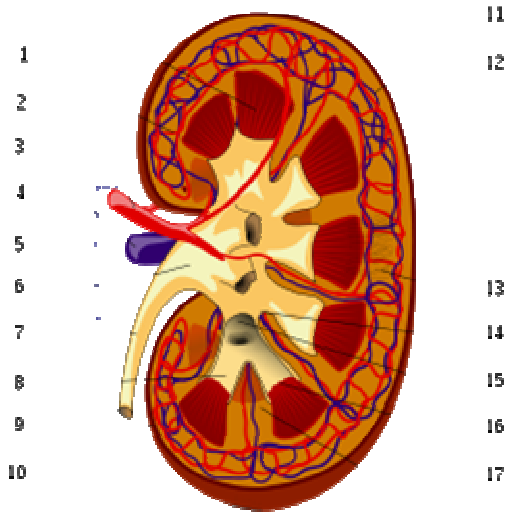
Blood supply:

The kidneys receive blood from the renal arteries, left and right, which branch directly from the abdominal aorta. Despite their relatively small size, the kidneys receive approximately 20% of the cardiac output. Each renal artery branches into segmental arteries, dividing further into interlobar arteries which penetrate the renal capsule and extend through the renal columns between the renal pyramids. The interlobar arteries then supply blood to the arcuate arteries that run through the boundary of the cortex and the medulla. Each arcuate artery supplies several interlobular arteries that feed into the afferent arterioles that supply the glomeruli. The interstitum (or interstitium) is the functional space in the kidney beneath the individual filters (glomeruli) which are rich in blood vessels. The interstitum absorbs fluid recovered from urine. Various conditions can lead to scarring and congestion of this area, which can cause kidney dysfunction and failure ***(Walter et al., 2004).***

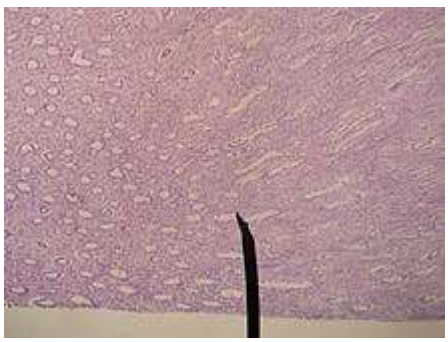
Histology:

Renal histology studies the structure of the kidney as viewed under a microscope. Various distinct cell types occur in the kidney, including ***(Bard et al., 2003):***

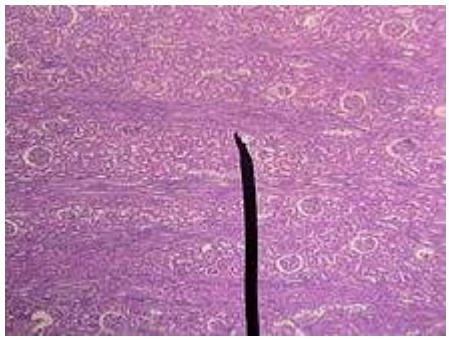
- Kidney glomerulus parietal cell
- Kidney glomerulus podocyte
- Kidney proximal tubule brush border cell
- Loop of Henle thin segment cell
- Thick ascending limb cell
- Kidney distal tubule cell
- Kidney collecting duct cell
- Interstitial kidney cells



1. Renal pyramid • 2. Interlobular artery • 3. Renal artery • 4. Renal vein 5. Renal hilum • 6. Renal pelvis • 7. Ureter • 8. Minor calyx • 9. Renal capsule • 10. Inferior renal capsule • 11. Superior renal capsule • 12. Interlobular vein • 13. Nephron • 14. Minor calyx • 15. Major calyx • 16. Renal papilla • 17. Renal column



Microscopic photograph of the renal medulla



Microscopic photograph of the renal cortex

Figure (1): Structure and histology of the kidney ***(Walter, 2004).***

Innervation:

The kidney and nervous system communicate via the renal plexus, whose fibers course along the renal arteries to reach the kidney. Input from the sympathetic nervous system triggers vasoconstriction in the kidney, thereby reducing renal

blood flow. The kidney is not thought to receive input from the parasympathetic nervous system. Sensory input from the kidney travels to the T10-11 levels of the spinal cord and is sensed in the corresponding dermatome. Thus, pain in the flank region may be referred from the kidney ***(Bard et al., 2003).***

How the kidney work?

The kidneys perform the essential function of removing waste products from the blood and regulating the water fluid levels. The diagram below shows the basic structure of the kidney. The kidneys receive blood through the renal artery. The blood is passed through the structure of the kidneys called nephrons, where waste products and excess water pass out of the blood stream, as shown in figure 2.

Functions:

Renal physiology

The kidney participates in whole-body homeostasis, regulating acid-base balance, electrolyte concentrations, extracellular fluid volume, and regulation of blood pressure. The kidney accomplishes these homeostatic functions both independently and in concert with other organs, particularly those of the endocrine system. Various endocrine hormones coordinate these endocrine functions; these include renin, angiotensin II, aldosterone and antidiuretic hormone.

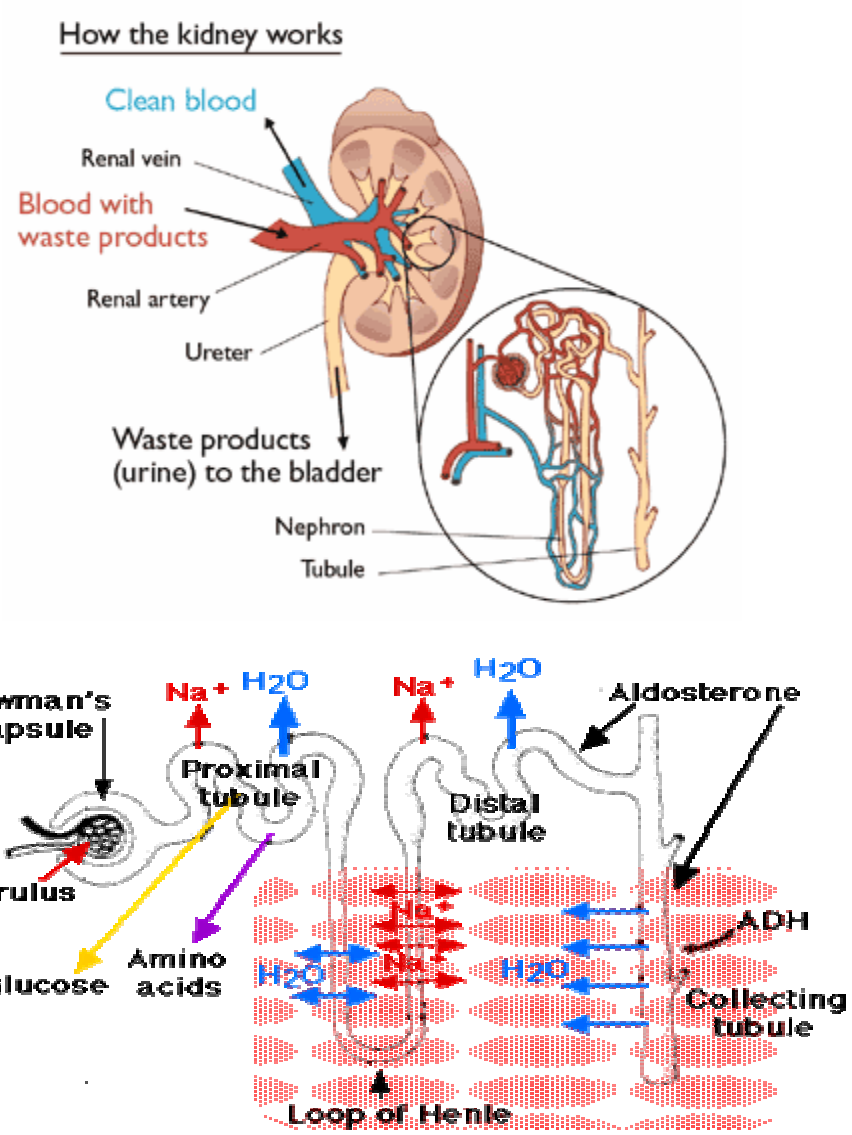


Figure (2): How the kidney works ***(Bard et al., 2003).***

Many of the kidney's functions are accomplished by relatively simple mechanisms of filtration, reabsorption, and secretion, which take place in the nephron. Filtration, which takes place at the renal corpuscle, is the process by which cells and large proteins are filtered from the blood to make an

ultrafiltrate that eventually becomes urine. The kidney generates 180 liters of filtrate a day, while reabsorbing a large percentage, allowing for the generation of only approximately 2 liters of urine. Reabsorption is the transport of molecules from this ultrafiltrate and into the blood. Secretion is the reverse process, in which molecules are transported in the opposite direction, from the blood into the urine ***(Stewart, 1998)***.

1- Excretion of wastes.

The kidneys excrete a variety of waste products produced by metabolism. These include the nitrogenous wastes called "urea", from protein catabolism, as well as uric acid, from nucleic acid metabolism. Formation of urine is also the function of the kidney.

2- Acid-base homeostasis.

Two organ systems, the kidneys and lungs, maintain acid-base homeostasis, which is the maintenance of pH around a relatively stable value. The lungs contribute to acid-base homeostasis by regulating bicarbonate (HCO_3^-) concentration. The kidneys have two very important roles in maintaining the acid-base balance: to reabsorb bicarbonate from urine, and to excrete hydrogen ions into urine ***(Corey, 2003).***

3- Osmolality regulation.

Any significant rise in plasma osmolality is detected by the hypothalamus, which communicates directly with the

posterior pituitary gland. An increase in osmolality causes the gland to secrete antidiuretic hormone, resulting in water reabsorption by the kidney and an increase in urine concentration. The two factors work together to return the plasma osmolality to its normal levels.

Antidiuretic hormone binds to principal cells in the collecting duct that translocate aquaporins to the membrane, allowing water to leave the normally impermeable membrane and be reabsorbed into the body by the vasa recta, thus increasing the plasma volume of the body ***(Candela and Yucha, 2007)***.

There are two systems that create a hyperosmotic medulla and thus increase the body plasma volume: Urea recycling and the 'single effect.'

Urea is usually excreted as a waste product from the kidneys. However, when plasma blood volume is low and antidiuretic hormone, is released the aquaporins that are opened are also permeable to urea. This allows urea to leave the collecting duct into the medulla creating a hyperosmotic solution that 'attracts' water. Urea can then re-enter the nephron and be excreted or recycled again depending on whether antidiuretic hormone, is still present or not.

The 'Single effect' describes the fact that the ascending thick limb of the loop of Henle is not permeable to water but is permeable to NaCl. This allows for a countercurrent exchange system whereby the medulla becomes increasingly concentrated, but at the same time setting up an osmotic

gradient for water to follow should the aquaporins of the collecting duct be opened by antidiuretic hormone.

4- Blood pressure regulation.

Long-term regulation of blood pressure predominantly depends upon the kidney. This primarily occurs through maintenance of the extracellular fluid compartment, the size of which depends on the plasma sodium concentration. Although the kidney cannot directly sense blood pressure, changes in the delivery of sodium and chloride to the distal part of the nephron alter the kidney's secretion of the enzyme renin. When the extracellular fluid compartment is expanded and blood pressure is high, the delivery of these ions is increased and renin secretion is decreased. Similarly, when the extracellular fluid compartment is contracted and blood pressure is low, sodium and chloride delivery is decreased and renin secretion is increased in response.

Renin is the first in a series of important chemical messengers that comprise the renin-angiotensin system. Changes in renin ultimately alter the output of this system, principally the hormones angiotensin II and aldosterone. Each hormone acts via multiple mechanisms, but both increase the kidney's absorption of sodium chloride, thereby expanding the extracellular fluid compartment and raising blood pressure. When renin levels are elevated, the concentrations of angiotensin II and aldosterone increase, leading to increased sodium chloride reabsorption, expansion of the extracellular

fluid compartment, and an increase in blood pressure. Conversely, when renin levels are low, angiotensin II and aldosterone levels decrease, contracting the extracellular fluid compartment, and decreasing blood pressure.

5- Hormone secretion.

The kidneys secrete a variety of hormones, including erythropoietin, and the enzyme renin. Erythropoietin is released in response to hypoxia (low levels of oxygen at tissue level) in the renal circulation. It stimulates erythropoiesis (production of red blood cells) in the bone marrow. Calcitriol, the activated form of vitamin D, promotes intestinal absorption of calcium and the renal reabsorption of phosphate. Part of the renin-angiotensin-aldosterone system, renin is an enzyme involved in the regulation of aldosterone levels ***(Rouiller et al., 1971).***

Glomerular filtration rate (GFR):

It is the volume of fluid filtered from the renal glomerular capillaries into the Bowman's capsule per unit time. Central to the physiologic maintenance of GFR is the differential basal tone of the afferent and efferent arterioles. It can be calculated by measuring any chemical that has a steady level in the blood, and is freely filtered but neither reabsorbed nor secreted by the kidneys. The rate therefore measured is the quantity of the substance in the urine that originated from a calculable volume of blood. Relating this principle to the below equation - for the substance used, the product of urine

concentration and urine flow equals the mass of substance excreted during the time that urine has been collected. This mass equals the mass filtered at the glomerulus as nothing is added or removed in the nephron. Dividing this mass by the plasma concentration gives the volume of plasma which the mass must have originally come from, and thus the volume of plasma fluid that has entered the bowman's capsule within the aforementioned period of time. The GFR is typically recorded in units of *volume per time*, e.g., milliliters per minute ml/min. Compare to filtration fraction ***(Guyton et al., 2006).***

$$GFR = \frac{\text{Urine Concentration} \times \text{Urine Flow}}{\text{Plasma Concentration}}$$

Normal ranges

The normal range of GFR, adjusted for body surface area, is similar in men and women, and is in the range of 100-130 ml/min/1.73m^2. In children, GFR measured by inulin clearance remains close to about 110 ml/min/1.73m^2 down to about 2 years of age in both sexes, and then it progressively decreases. After age 40, GFR decreases progressively with age, by about 0.4 - 1.2 mL/min per year ***(Stevens et al., 2008).***

Renal replacement therapy

Renal replacement therapy (RRT) replaces nonendocrine kidney function in patients with renal failure and is occasionally used for some forms of poisoning. Techniques include intermittent hemodialysis, continuous hemofiltration and hemodialysis, and peritoneal dialysis. All modalities exchange solute and remove fluid from the blood, using dialysis and