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NURSING SCIENCE

200 level

PHYSIOLOGY 212

DISCUSSION THE URINE FORMATION AND CONCENTRATION.

Formation of urine is a process important for the whole organism. Not only acid-base balance is modulated by it, but also blood osmolarity, plasma composition and fluid volume, and thus it influences all cells in our body.

A healthy adult person produces 1.5-2 liters of urine per day and this process involves three basic mechanisms:

1) Glomerular filtration

2) Tubular reabsorption

3) Tubular secretion

GLOMERULAR FILTRATION.

The volume of liquid filtered per unit time in all glomeruli can be expressed as the glomerular filtration rate (GFR). Its physiological value is 120 ml/min/1,73m2 body surface area, thus 180 l/day. About 99 % of the filtrate gets reabsorbed by the tubular resorption to the extracellular fluid (back into the body), leaving only 1.5-2 l of urine per day. Movement of the fluid through the filtration membrane is controlled and determined by the ratio of the hydrostatic pressure in the capillaries and oncotic pressure of plasma proteins (less by the hydrostatic pressure of the interstitial fluid and oncotic pressure in the filtrate). These forces are called Starling´s forces and there are a few differences from the general principles:

1) Fluid is not exchanged between the capillary and the interstitium, but between the capillary and the fluid of Bowman’s capsule

2) Hydrostatic pressure in the capillaries is different, the movement is thus only one-sided (in the direction of filtration)

3) Filtration barrier (see above) has a unique structure and properties which do not allow passage of proteins into the filtrate (primary urine)

GFR is therefore dependent on the renal blood flow, the filtration pressure, the plasma oncotic pressure, and the size of the filtration area.

Control of glomerular filtration

Its main determinant is the renal blood flow that is directly proportional to the pressure difference between renal artery and renal vein and inversely proportional to the peripheral resistance of the afferent and efferent arteriole and the interlobular artery. We distinguish local and central regulatory mechanisms.

If we want to determine GFR, which is one of the basic function of our kidneys, we have to use a substance that is excreted from the body only by glomerular filtration (inulin, creatinine) and is not affected by tubular processes. As an example we can mention the calculation of the clearance (plasma volume that is per unit time completely cleaned of marker substances) of endogenous creatinine, whose formula has the following form:

Vypocet GF

U – urine creatinine concentration in mmol/l

V – volume of urine (diuresis) in ml/s

P – plasma creatinine concentration in mmol/l

In clinical practice, we use more complex calculations, corrected for body surface area (and other physical parameters) – e.g. equation by Cockroft and Gault, equation MDRD etc.

Tubular reabsorption and secretion

As we mentioned above, about 99 % of the filtrate gets reabsorbed by the tubular resorption to the extracellular fluid (back into the body), leaving only 1.5-2 l of urine per day. The main task for renal tubules is therefore an isosmotic tubular reabsorption of primary urine. They absorb water, ions (sodium, chlorides, potassium, calcium, magnesium, bicarbonate or phosphate), urea, glucose and amino acids. All of this is independent on the extracellular fluid volume in the body – we speak about the obligatory resorption. Its primary role is to maintain fluid volume in the body under normal conditions.

Transport can be carried by passive diffusion (in the direction of the concentration or electrical gradient), primary active transport against gradient (needs energy – ATP) or secondary active transport (transport protein uses the concentration gradient created by a primary active transport realized by other transport protein). Substances can be transported by paracellular or transcellular routes. Transport of water is always passive. Na+/K+-ATPase located on the basolateral membrane plays important role in the secondary active transport. It creates a concentration gradient for Na+. Transport proteins act as symporters (transport of compound is coupled to the transport of Na+ in the same direction) or antiporters (transport of compound is coupled to the transport of Na+ in the opposite direction). To understand the processes in the tubular system, we must imagine tubular epithelial cells, their apical membrane facing the tubular fluid (primary urine), basolateral membrane, on the other hand, is in contact with the peritubular fluid (here is located the Na+/K+-ATPase).

Souhrn procesů tvorby moci ENG-01

The proximal tubule

Reabsorption of sodium ions is in the first half of the proximal tubule coupled with the reabsorption of bicarbonate, glucose, amino acids, lactate, urea and phosphate. Absorbed compounds are osmotically active, thereby draining water from tubules. This leads to an increased concentration of chloride ions in the tubular fluid that is very important for a resorption in other parts of the proximal tubule.

Reabsorption of bicarbonate ions in the proximal tubule

Movement of bicarbonate and hydrogen ions depends on the transport sodium ions. This process is catalyzed by enzyme carbonic anhydrase (located in the apical membrane and in the intracellular part of the epithelial cells). The first step is the secretion of H+ into the tubular fluid through the Na+/H+ antiport, located at the luminal (apical) membrane of proximal tubule cells. Transferred H+ may in the tubular fluid react with filtered bicarbonate ions to form carbonic acid. Carbonic anhydrase facilitates the decomposition of carbonic acid in the tubular fluid to water and carbon dioxide. Both compounds can freely diffuse into the tubule epithelial cells, where carbonic acid is restored by the carbonic anhydrase. Molecules of carbonic acid dissociates into hydrogen and bicarbonate ions. Bicarbonate ions then pass through the basolateral membrane into the interstitial fluid through Na+/3HCO3–-cotransporter or anion exchanger (Cl–/HCO3–). H+ returns via antiport with Na+ into the tubular fluid. For each secreted H+, Na+ and HCO3– is absorbed (Na+ is returned to the blood by active transport in exchange for K+ – Na+/K+-ATPase).

Renal (tubular) threshold

Glucose, amino acid and many other organic compounds are in this part of the tubule completely resorbed under physiological conditions. This transport has some maximum value – so-called renal/tubular threshold. As an example we can mention the renal threshold for glucose. When this renal threshold is exceeded (due to too high plasma concentration – such as 10 mmol/l for glucose), glucose reabsorption in the proximal tubule is incomplete and some amount of glucose remains in the final urine. Unabsorbed osmotically active molecules drain water molecules to renal tubules, thereby increasing diuresis (osmotic polyuria).

Reabsorption of sodium ions is in the second half of the proximal tubule coupled with the transport of chloride ions, used are both transcellular (on basolateral membrane helps K+/Cl–-symport) and paracellular routes. Relatively abundant positively charged ions (sodium, potassium, calcium, magnesium) in the tubular fluid accompany chloride ions in paracellular transport. Transport of ions is followed by passive reabsorption of water.

Loop of Henle

Henle’s loop absorbs about 25 % of the solutes (thick segment of the ascending limb), but only about 15 % water (descending limb). Its proper function (thick part of the ascending limb is impermeable to water and has active transport of Na+ and Cl–) is essential for the formation of a high osmotic pressure (hyperosmolarity) in the renal medulla that ensures a production of highly concentrated urine. Some mechanisms of reabsorption of ions are similar to those in the proximal tubule. Very important is the specific symport of Na+, K+ and 2 Cl– across the apical membrane. This symport uses energy derived from the transport of sodium and chloride ions in the direction of their concentration gradient for the transport of potassium ions into the cell (against their concentration gradient). Some of these ions leave cells on the basolateral membrane (together with Cl–), some return back into the tubular fluid, thereby creating an electrical imbalance. Due to this, positively charged ions (Na+, K+, Ca2+, Mg2+) are resorbed by paracellular route (very important mechanism for resorption of solutes). This is especially significant for formation of a hypertonic renal medulla. Hypotonic fluid leaves the loop of Henle and enters the distal tubule.

TUBULAR SECRETION

The only difference between secretory and re absorptive tubular mechanisms lies in the direction of transport; secretory mechanisms involve the addition of substances to the filtrate from the plasma in the peritubular capillaries. The small amount of secretion that does occur, except for the secretion of potassium and uric acid, takes place in the proximal tubule. Hydrogen ions are also secreted and ammonia is generated, but they are special cases and are discussed below under Regulation of acid-base balance. As in the case of reabsorption, secretion occurs both passively and actively against an electrochemical gradient.

Several drugs are actively secreted, and some of these appear to share a common pathway so that they may compete with each other for a limited amount of energy. This may be turned to therapeutic advantage in the case of penicillin, which is eliminated partly by tubular secretion. The drug probenecid, which can be given simultaneously, competes with penicillin at its secretory site and thus helps to raise the level of penicillin in the blood in the treatment of certain infections. Endogenous (originating within the body) compounds that are secreted also include prostaglandins, bile salts, and hippurate. Uric acid derived from nucleoproteins freely passes the glomerular barrier and is normally largely reabsorbed in the proximal tubule. In some circumstances, however, it is also secreted by other parts of the same convoluted tubule.

The concentration of urine

As already indicated, the loop of Henle is critical to the ability of the kidney to concentrate urine. The high concentration of salt in the medullary fluid is believed to be achieved in the loop by a process known as countercurrent exchange multiplication. The principle of this process is analogous to the physical principle applied in the conduction of hot exhaust gases past cold incoming gas so as to warm it and conserve heat. That exchange is a passive one, but in the kidney the countercurrent multiplier system uses energy to “pump” sodium and chloride out of the ascending limb of the loop into the medullary fluid. From there it enters (by diffusion) the filtrate (isotonic with plasma) that is entering the descending limb from the proximal tubule, thus raising its concentration a little above that of plasma. As this luminal fluid in turn reaches the ascending limb, and subsequently the distal tubule, it in turn provides more sodium to be pumped out into the surrounding fluid or blood, if necessary, and transported (by diffusion) back into the descending limb; this concentrating process continues until the osmotic pressure of the fluid is sufficient to balance the resorptive power of the collecting ducts in the medulla, through which all of the final urine must pass. This resorptive capacity in the ducts is regulated by antidiuretic hormone (ADH), which is secreted by the hypothalamus and stored in the posterior pituitary gland at the base of the brain. In the presence of ADH, the medullary collecting ducts become freely permeable to solute and water. As a consequence, the fluid entering the ducts (en route to the renal pelvis and subsequent elimination) acquires the concentration of the interstitial fluid of the medulla; i.e., the urine becomes concentrated. On the other hand, in the absence of ADH, the collecting ducts are impermeable to solute and water, and, thus, the fluid in the lumen, from which some solute has been removed, remains less concentrated than plasma; i.e., the urine is dilute.