Why does the plasma urea concentration increase in acute dehydration?

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Acute dehydration biochemically manifests itself with mild uremia and a normal creatinine concentration. The reason for this, as quoted in popular medical textbooks, is that there is increased reabsorption of urea by the kidneys (1). This explanation is rarely taken further by clinical tutors or lectures on laboratory medicine. However, an appreciation of the physiology of the renal tubules allows one to understand two important points: 1) why the plasma urea concentration is in any way related to changes in blood volume and 2) the teleology of the phenomenon (2). The latter dispels the myth that the effect is in someway mysterious or purposeless.

Both the thin ascending limb of the loop of Henle and the inner medullary collecting duct are relatively permeable to urea, whereas the thin descending and thick ascending limbs of the loop of Henle, the distal tubule, and early parts of the collecting system are relatively impermeable to urea. The reabsorption of water along the nephron thus leads to a rise in the tubular urea concentration. During hypovolemia, when levels of vasopressin are high and water is maximally reabsorbed, the inner medullary interstitial fluid urea concentration concomitantly rises, owing to the increased concentration gradient for the passive transport of urea out of the collecting duct system. This effect is enhanced because urea transporter UT-A1 in the inner medullary collecting duct is directly sensitive to vasopressin and upregulates its expression (3). Thus, the increased steady-state level of urea in the plasma of acutely dehydrated patients is a reflection of the increased urea concentration in the medullary interstitium, owing to a vasopressin-mediated elevation in urea reabsorption in the collecting ducts.

The adaptive effect of this increased reabsorption of urea is to potentiate the effect of vasopressin, thereby allowing for the greater retention of water from the filtrate. The urea reabsorbed increases the medullary concentration of the solute, which is critical for the reabsorption of water from the thin inner medullary part of the descending limb of the loop of Henle. Here, there is no osmotic gradient to cause water movement in the diluting kidney. Thus, in the presence of vasopressin, and therefore a significant medullary urea concentration, there is passive reabsorption of salt from the thin ascending limb, because the salt concentration of the tubular fluid flowing up from the apex of the loop is higher than that of the surrounding medullary fluid. Without the reabsorption of urea, the osmotic gradient for water reabsorption in the descending limb would not extend below the thick segment, and, in the concentrating human kidney, urea handling can account for half of the osmotic pressure of the medullary fluids. In fact, to keep urea movements intact, some urea diffuses into the thin ascending limb, allowing it to be recycled. In the absence of vasopressin, the medullary urea concentration gradually dissipates.

REFERENCES