Test Your Knowledge: Diuretic Resistance

Diuretic therapy is commonly employed in nephrology practice. Diuretic resistance, however, can be seen especially in patients with chronic edematous conditions such as nephrotic syndrome, heart failure, liver cirrhosis, and advanced chronic kidney disease (CKD). In a recent *AJKD* article, Hoorn and Ellison review a case of nephrotic syndrome and diuretic resistance. The clinical approach to patients with diuretic resistance is also discussed. Test your knowledge on diuretic resistance in the following quiz.

1. In patients with nephrotic syndrome who have developed resistance to the diuretic action of 160 mg/day oral furosemide, which of the following is the best next step in producing a natriuresis?
    A. Continue with current diuretic dose
    B. Increase the dose of furosemide
    C. Add another diuretic agent
    D. Admit the patient to a hospital for intravenous diuretic therapy

2. In patients with nephrotic syndrome, which of the following can be the cause of diuretic resistance?
    A. Hypoalbuminemia
    B. Intrarenal edema
    C. Poor intestinal absorption
    D. All of the above

3. Among the following loop diuretics, which one has the lowest bioavailability?
    A. Torsemide
    B. Furosemide
    C. Bumetanide

4. A patient with congestive heart failure and apparent diuretic resistance is admitted to the hospital because of worsening edema. He has been treated with torsemide and metolazone but recently has begun to gain weight despite strict adherence to medication use and diet. Which of the following additional diuretic agents would be effective in improving his response to therapy?
    A. Triamterene
    B. Bumetanide
    C. Acetazolamide
    D. Chlorthiazide

*Quiz prepared by **Hitesh H. Shah**, AJKD Blog Contributor*

To view the Hoorn and Ellison Teaching Case **abstract** or **full-text** (subscription required), please visit **AJKD.org**.

Solutions to *AJKD* Blog's Test Your Knowledge: Diuretic Resistance

1. **C. Add another diuretic agent**

   In the flowchart outlined in this article, adding a synergistic diuretic that works at an alternative site is the preferred next step prior to hospitalizing the patient for intravenous or continuous infusions.

2. **D. All of the above**

   There are many causes of diuretic resistance including medication compliance, salt intake, tubular secretion of the drug, and NSAID use. Additionally, nephrotic syndrome can lead to diuretic resistance due to poor oral absorption from mucosal edema of the intestine, decreased drug delivery due to hypoalbuminemia, and compromised glomerular hemodynamics from intrarenal edema ("nephrosarca").

3. **B. Furosemide**

   Despite being the most commonly used loop diuretic, furosemide has the lowest bioavailability (40-60%) compared to bumetanide (80%) or torsemide (>91%). Even when adequate plasma concentration of diuretic is achieved, it must be secreted adequately into the tubular lumen which can be compromised in edematous disorders because the diuretics are highly protein bound.

4. **A. Triamterene**

   The best next step is to inhibit a "downstream" sodium reabsorptive site using the ENaC channel blocker, triamterene. Since metolazone already inhibits a component of proximal tubular sodium handling, adding acetazolamide which also acts on the proximal tubule would add little further benefit. Metolazone also has an action on the NCC2 transporter in the distal nephron, adding chlorthiazide would also add little since it too acts on that transporter. Triamterene would add to diuretic action by blocking the activated ENaC transporter in the collecting tubule. This may be particularly useful in patients with nephrotic syndrome since they can develop avid sodium retention due to filtered plasmin leading to activation of the ENaC sodium transporter (primary renal sodium retention).

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