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CE - LETTER TO THE EDITOR

Prevalence and outcome of diuretic resistance in heart failure: comment

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Dear Editor,

It is with great interest that we read the paper by Trullàs et al. about diuretic resistance in heart failure [1]. As they state, it is prevalent and represents a major challenge in the management of patients with heart failure. Failure to respond to diuretic therapy appears to be a multifactorial phenomenon where major determinants play a main role. The amount of diuretic that reaches the nephron is an important factor; more than 90% of furosemide, which is the most frequently prescribed loop diuretic in the treatment of heart failure, travels through the bloodstream bounded to protein to reach the kidney, so hypoalbuminemia (frequently seen in cachectic patients with advanced heart failure) can compromise the amount of diuretic that is delivered. Moreover, oral furosemide bioavailability is highly variable (10–100%), and gut edema secondary to systemic congestion further impairs diuretic absorption. Time from diuretic administration to action in the kidney is also a determinant. In patients with heart failure, renal blood flow can be low, secondary to low cardiac output, delaying the time of diuretic delivery and contributing to resistance. Finally, high doses of diuretics eventually lead to nephron remodeling with hypertrophy and hyperplasia of the cells from the distal convoluted tubule, increasing its reabsorbing capacity which reduces natriuresis and contributes to resistance [2, 3]. This multifactorial nature makes diuretic resistance hard to define and recognize.

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Reliable assessment of congestion can only be achieved using invasive methods, which is unpractical and places the patients at risk for complications [4]. The combination of clinical findings along with chest X-ray, biomarkers, lung ultrasound and assessment of vena cava compressibility can allow an adequate diagnosis [3, 4]. Assessment of euvolemia can be even harder since the performance of clinical findings is not clear and there are no reliable bedside tests. Many patients that are thought to be euvolemic can be discharged from hospital with residual or subclinical congestion, and even those patients that have dyspnea relief with diuretic therapy can still have undetected residual congestion [3, 5]. So, defining the response to diuretics as the presence or absence of congestion can be imprecise. Other indicators of diuretic response like changes in body weight can also lack accuracy, since correlation between weight loss and urine output can be poor [3, 4]. Trullàs et al. divided their cohort into patients with or without diuretic resistance in heart failure; those considered with diuretic resistance were patients with heart failure symptoms even if daily dose of oral furosemide was at least 80 mg at home. Recently, the Heart Failure Association of the European Society of Cardiology released a statement of diuretic use in congestive heart failure, where they addressed some of the difficulties in the evaluation of these patients and gave recommendations for timely recognition and management of patients that are unresponsive to diuretics [3]. In this statement, authors give an algorithm for a stepped approach to patients with congestive heart failure. They suggest that measurement of urinary sodium along with urinary output after an initial dose of intravenous diuretics can be a more objective way to determine diuretic response. In this algorithm, spot urinary sodium is measured 1–2 h after an initial dose of loop diuretic, and urinary output is measured after 6 h of the initial dose. Those patients with urinary sodium > 50–70 meq/l (after 1–2 h) and urinary output of > 100–150 ml/hour (after 6 h) are thought to have an adequate response to

diuretics and need no incremental dose, while those that do not meet the criteria need incremental doses of diuretics with reassessment every 6 h until they show response or reach the maximum daily dose. Authors state that using this approach will allow clinicians to promptly detect unresponsive patients and to make timely adjustments in therapy.

In conclusion, the paper by Trullàs et al. gives us a great perspective about the burden and impact of diuretic resistance in patients with heart failure, and reminds us that there is still a long way to go in the recognition and management of these patients. We need a more accurate and homogeneous definition of diuretic resistance to make the inclusion of patients in clinical studies more precise. Also, it is unclear if patients that initially show response to diuretic will eventually develop resistance and if there are reliable predictors of this progression. Unfortunately, hospitalization for heart failure decompensations has a great impact on survival but is also a great opportunity for clinicians to optimize guideline-directed treatment to decrease the risk of recurrent hospitalizations, whether optimization of therapy in those patients with heart failure and diuretic resistance has any impact in the response to diuretics and a secondary impact in survival is also not clear.

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