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UPDATE I

Oral diuretic observation in patients with heart failure – futile?

A common practice in patients hospitalized with heart failure has been to monitor the response to oral diuretics after a period of intravenous (IV) diuresis. This practice has been called into question after an analysis of two large cohorts showed a paucity of clinically meaningful outcomes. The investigators analyzed in-hospital measures of diuretic response, clinicians' decisions, and diuretic response 30 days post-discharge in two cohorts: The Mechanism of Diuretic Resistance (MDR) and Yale multicenter cohorts.¹ In the MDR cohort, patients were, on average, 64 years old, 66% male, 62% white, and had an ejection fraction of 40%. Patients were admitted to hospital with acute decompensated heart failure, and to be included in the cohort, required treatment with IV loop diuretics for at least three days with a diuresis goal of at least one liter net negative per day and at least one objective sign of fluid overload.

As they were nearing discharge, the patients underwent a timed 6-hour urine collection after administering an oral loop diuretic, dosed at the physician discretion. Some then were discharged based on physician judgment while the others remained hospitalized and underwent a timed 18-hour collection and then, ideally, a 30-day post-discharge visit with a similar urine collection protocol. The diuretic response was measured by weight change, net fluid balance, and cumulative sodium excretion at both 6 and 24 hours.

Of the 468 patients in the MDR cohort, 57% (n=265) had observation on oral diuretic (OOD) as part of usual care, and 81% of these patients completed the 30-day post-discharge visit. Weight change and net fluid balance,

clinical parameters commonly used to evaluate clinical response to an oral diuretic, correlated poorly ($r=0.36$). Weight change and net fluid balance were only modestly correlated with sodium excretion ($r=0.41$ and $r=0.63$, respectively). Surprisingly, 80% of patients discharged on the day of the OOD were discharged on the same oral diuretic dose they received during the 6-hour urine collection, regardless of diuretic response ($P>0.30$). Conversely, most patients (71%) discharged after an OOD of 24 hours or more had their dose at discharge decreased. However, this decision to decrease the dose did not appear to be related to any meaningful clinical parameter. The only variable associated with the discharge loop dose was the preadmission home loop diuretic dose ($r=0.72$, $P<0.001$). The median length of stay (LOS) also tended to be higher in patients with OOD: 9 days versus 8 days, respectively ($P=0.23$).

Ninety-eight patients who had their in-hospital oral diuretic natriuretic response quantitated returned for their 30-day visit, revealing that in-hospital cumulative sodium excretion was only modestly correlated with sodium excretion at the outpatient visit ($r=0.26$, $P=0.02$); i.e., most of the variation in the outpatient natriuresis was not explained by the in-hospital natriuresis. Cumulative natriuresis nearly doubled from the in-hospital to the outpatient visit on a population level, which the authors state was not driven by post-discharge diuretic dose up-titration as only 14% received higher doses.

The Yale multicenter cohort was a retrospective analysis of five institutions at the Yale New Haven Healthcare system in Connecticut, United States of America, where the primary outcome was 30-day readmission. They included a total of 18,454 heart failure hospitalizations from 10,408 patients. This cohort received IV loop diuretics during the first 24 hours of admission and any oral loop diuretic within the 24 hours before discharge

($n=10,150$ for oral loop diuretics prior to discharge). The average age was 76 years, 51% were male, and 75% were white. Receiving oral diuretics within 24 hours of discharge was not associated with 30-day readmission (HR, 0.98 [95% CI, 0.93–1.05]; $P=0.61$). Similarly, within the MDR cohort, having an in-hospital OOD was not associated with a lower risk of HF readmission [HR, 1.02 (95% CI, 0.78–1.34; $P=0.88$)].

Take-away: Observing hospitalized patients with heart failure on an oral diuretic likely does not result in clinical benefit. The clinical data obtained from this practice is often discrepant and not acted upon by clinicians. The natriuretic response observed while inpatient does not correlate with the outpatient diuretic response. OOD does not reduce hospital readmissions and likely increases LOS. Clinicians should continue to recommend timely outpatient follow-up and adherence to a low sodium diet and oral diuretic regimen.

UPDATE 2

Corticosteroids reduce mortality in severe community acquired pneumonia

When and if corticosteroids should be used in community-acquired pneumonia (CAP) is a controversial, and a recent systematic review and meta-analysis provide some much-needed clarification.² Investigators searched several databases in an unrestricted fashion, including updated clinical trial updates, from February 2020 to September 2022. Studies were eligible if they randomized adult patients hospitalized with probable or suspected *bacterial* CAP of all severities to treatment with corticosteroids versus standard care or placebo. Trials were defined as more severe if $\geq 50\%$ of the participants had severe pneumonia scores (pneumonia severity scores (PSI) of IV or V, CURB65 scores of ≥ 3 , CORB scores of ≥ 2 , or if $\geq 50\%$ of patients were admitted to the intensive care unit (ICU) at the time of randomization). Outcomes of interest included mortality, need for invasive mechanical ventilation, secondary infections, gastrointestinal (GI) bleeding of any severity, ICU admission (in those not requiring the ICU admission at baseline), hyperglycemia requiring intervention, and ICU and hospital stay duration. Data were collected at the longest follow-up or closest to 90 days.

The researchers identified 18 trials that included 4661 patients with a median age of 64. 71% of patients were male. Ten trials were classified as “severe disease” with significant heterogeneity between trials. About 1/3 of patients were admitted to the ICU, 10% received invasive mechanical ventilation, and 4.6% had septic shock. The median total corticosteroid dose used was approximately 70 mg of dexamethasone equivalent (for a daily dose of approximately 10 mg of dexamethasone equivalent/day). Seventeen trials (4567 patients) reported mortality, with

443 deaths. Seven trials (43.7% of patients) were at probable/high risk of bias. For patients with more severe pneumonia, corticosteroids probably reduced mortality as compared to usual care (RR 0.62 [95% CI 0.45 to 0.85]; moderate certainty), with an absolute risk difference of 56 fewer deaths per 1000 patients [95% CI 81 to 22 fewer]. For patients with less severe pneumonia, corticosteroids may have no effect on mortality compared to usual care (RR 1.08 [0.83 to 1.42]; low certainty).

Corticosteroids probably reduced the need for invasive mechanical ventilation compared to usual care (RR 0.56 [0.42 to 0.74]; moderate certainty) and the need for ICU admission (RR 0.65 [0.43 to 0.97]; moderate certainty). Corticosteroids may reduce the duration of hospitalization and ICU stay; however, the evidence supporting this was of low certainty. The highest impact on mortality was seen with an optimal dose of approximately 6 mg of dexamethasone equivalent daily for seven days (RR 0.45 [95% CI 0.32 to 0.68]). The corticosteroid regimens used were heterogenous; however, there was a subgroup difference favoring hydrocortisone (most often given as IV bolus, followed by a continuous infusion for seven days) compared to other corticosteroids (moderate/low certainty). Corticosteroids had no evident effect on the risk of secondary infections (RR 1.09 [95% CI 0.85 to 1.41]; low certainty) or gastrointestinal bleeding (RR 0.95 [95% CI 0.56 to 1.60]; low certainty) but probably increased the risk of hyperglycemia when compared to usual care (RR 1.76 [95% CI 1.46 to 2.14]; moderate certainty).

Take-away: In patients with severe bacterial CAP, dexamethasone 6mg daily for seven days (or corticosteroid equivalent) probably reduces mortality, the need for ICU admission, and mechanical ventilation.

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The author declares they have no conflicts of interest

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- Substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work; AND
- Drafting the work or revising it critically for important intellectual content; AND
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- Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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