Tolvaptan in the very elderly with acute decompensated heart failure- a therapeutic option worth of consideration

Acute decompensated heart failure (ADHF) is a common and potentially fatal event in the natural history of heart failure that is associated with a greater risk of mortality and rehospitalization compared with stable heart failure (1). Elderly patients represent an important fraction of patients with ADHF, and these patients are at higher risk for in-hospital mortality and require a longer hospital stay to stabilize the condition compared with younger patients (2). Acute congestion related to rapid fluid accumulation and increased venous pressure is a constant finding and a major target of acute therapy in patients with ADHF (3). Loop diuretics remain the mainstay decongestive therapy in patients with ADHF (4). However, the benefits of these agents are limited by diuretic resistance, neurohormonal activation, electrolyte disturbance, or worsening of renal function (WRF) (4). Randomized studies have shown that the oral vasopressin-2 receptor antagonist tolvaptan reduces congestion and relieves symptoms in patients with ADHF (5, 6). Tolvaptan promotes electrolyte-free water excretion (aquaresis) and is indicated in hypervolemic (or euvolemic) states associated with hyponatremia (7). The drug does not appear to adversely affect renal function or cause neurohormonal activation (8). The evidence on the use of tolvaptan in elderly patients with ADHF is limited (9, 10).

In this issue of the Anatolian Journal of Cardiology, the article entitled "The clinical utility of early use of tolvaptan in very elderly patients with acute decompensated heart failure" by Niikura et al. (11) assessed the safety and efficacy of early use (within 24 hours of hospitalization) of oral tolvaptan in very elderly (≥85 years of age; n=45) versus younger patients (<85 years; n=66) with ADHF. The primary outcome was WRF (creatinine increase >0.3 mg/dL from admission level) or severe WRF (creatinine increase >0.5 mg/dL from admission level). Secondary outcomes included in-hospital death and hospitalization time. The mean tolvaptan dose (7.4 mg/day vs. 7.5 mg/day) or duration (4.3 days vs. 5.4 days) did not differ significantly in the very elderly versus the patients of a younger age. Of note, the incidence of WRF (primary outcome) and in-hospital death and mean hospital stay duration (secondary outcomes) did not differ in the very elderly vs. the patients of a younger age. From these results, it may be concluded that early initiated and short duration therapy with tolvaptan is comparably safe and efficacious in both the very elderly and younger patients with ADHF.

The authors are to be commended for performing this study. The study has a well-grounded rationale and is rich in mechanisms offered to explain the findings. The treatment of ADHF in the (very) elderly can be particularly difficult due to advanced age-related frailty and comorbidities increasing the odds for a poor outcome, deterioration of liver and kidney function predisposing to inadequate drug metabolism or elimination, reduced efficacy, and increased risk of drug toxicity, or other adverse events. In this regard, this study (11) is reassuring in that, regardless of age, tolvaptan represents a safe therapy for patients with ADHF. More specifically, tolvaptan use in doses and duration as used in the study performed by Niikura et al. (11) does not increase the risk of WRF, a relatively common side effect of drug therapy in patients with ADHF that portends a poor prognosis (12). Moreover, the study may be unique in addressing the treatment of ADHF in such a high-risk and difficult to treat group of patients as are the very elderly.

The authors are correct in recognizing the small sample size, lack of a unified protocol with respect to the timing of tolvaptan initiation and discontinuation, lack of a comparator group without tolvaptan, and the short observational period, which does not allow for assessing post-discharge outcomes like the need for rehospitalization, as limitations of the study. Two additional limitations, the lack of a randomized design and not assessing the impact of tolvaptan on clinical parameters used to evaluate (de)congestion, such as weight loss and dyspnea relief, are also worth mentioning. Despite these weaknesses, the main study findings and the clear message from this study that tolvaptan is a safe and beneficial drug to treat congestion in elderly patients with ADHF remain uncompromised. Specifically designed, randomized, controlled studies are needed to corroborate these findings and determine the role of tolvaptan in the treatment of elderly patients with ADHF.

Gjin Ndrepepa
Department of Adult Cardiology, Deutsches Herzzentrum München, Technical University; Munich-*Germany*

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Address for correspondence: Gjin Ndrepepa, MD, Deutsches Herzzentrum München, Lazarettstrasse 36 80636 München-*Germany*
Phone: +49-89-12181535 Fax: +49-89-12184053 E-mail: ndrepepa@dhm.mhn.de
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