Use of Oral Furosemide in Hemodialysis

To the Editor: We read with interest the paper by Flythe *et al.*[1] that examines the efficacy, safety, and tolerability of oral furosemide in patients undergoing hemodialysis. We congratulate the authors for conducting this useful and long-needed study that consisted of a 6-week dose titration period and a 12-week follow-up period. The maximum furosemide dose for any participant was 320 mg/d. Flythe *et al.*[1] conclude that furosemide was generally safe and well tolerated.

In this regard, we would like to share information about our practice[2,3] using higher doses and for a longer time. Initially, it was needed to establish a maximal effective dose for incident patients. To this end, we conducted a crossover, single-blind study. Thirty-four patients were randomly assigned to receive 250 mg or 500 mg of oral furosemide once a day for 1 week. Effect of both doses on urine output was similar. Both increased 24-hour urinary volume by 30%. In contrast, sodium excretion was significantly higher with 500 mg. Subsequently, daily urine output was measured in all incident patients. The patients with daily urine output higher than 200 ml a day received 500 mg of oral furosemide once a day. After 11.8 $\pm$ 4.7 months, 33 incident patients were able to preserve their baseline residual urine output and their excretion of sodium and phosphorus. Serum β_2-microglobulin was significantly lower than β_2-microglobulin measured in control patients. There were no significant changes in serum levels of potassium and calcium. Only 4 patients experienced adverse events. One experienced cramps and 4 experienced rash and pruritus. All symptoms improved when furosemide was discontinued. No patient reported changes in their hearing.

These preliminary results[2,3] support the conclusions of Flythe *et al.*[1]; high doses of furosemide are effective, safe, and well tolerated in patients undergoing hemodialysis. Furthermore, well-designed randomized controlled trials are needed to verify these findings.

1. Flythe JE, Assimon MM, Tugman MJ, et al. Efficacy, safety, and tolerability of oral furosemide among patients receiving hemodialysis: a pilot study. *Kidney Int Rep*. 2022;7:2186–2195. https://doi.org/10.1016/j.ekir.2022.07.003
2. Alcuaz R, Nozzi E, Vivas N, Diaz G, Aiziczon D, Siga E. The preservation of residual renal function with high dose of furosemide. A pilot long-term study. *Nephrol Dial Transplant*. 2019;34(suppl 1). https://doi.org/10.1093/ndt/gfz106.FP683. gfz106.FP683.
3. Siga E, Alcuaz R, Nozzi E, et al. Survival and residual kidney function in hemodialysis patients treated with high doses of furosemide. A prospective long-term study. *Nephrol Dial Transplant*. 2020;1755(suppl 3). https://doi.org/10.1093/ndt/gfaa1. gfaa142.P1441.

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Response to "Use of Oral Furosemide in Hemodialysis"

The Authors Reply: We thank Siga and Alcuaz for their interest in our study that examines the efficacy, safety, and tolerability of oral furosemide among individuals treated with maintenance hemodialysis.[1,2] The authors share their experience in Argentina of administering oral furosemide at doses of 500 mg/d to incident hemodialysis patients with daily urine output of >200 ml. They observed maintenance of urine output with minimal side effects after nearly a year of follow-up under this regimen. Their preliminary report, in combination with our data, support the need for larger trials testing the effectiveness of furosemide for improving volume-related outcomes among patients treated with hemodialysis. In addition, taken together, they underscore the importance of incorporating into future furosemide trials such design features as a pre-randomization run-in phase to assess for furosemide response and tolerance.

1. Flythe JE, Assimon MM, Tugman MJ, et al. Efficacy, safety, and tolerability of oral furosemide among patients receiving hemodialysis: a pilot study. *Kidney Int Rep*. 2022;7:2186–2195. https://doi.org/10.1016/j.ekir.2022.07.003

2. Siga E, Alcuaz R. Use of oral furosemide in hemodialysis. *Kid Int Rep*. 2023;8:206–207.

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